

Age, Genetics Affect PD Risk in Pesticide Exposure

BY JEFF EVANS

The risk for developing Parkinson's disease that is associated with pesticide exposure appears to be especially high in people who are professionally exposed to the chemicals and those who carry certain polymorphisms for glutathione S-transferase genes, according to data from two new case-control studies.

The studies strengthen the already well-documented association between pesticide exposure and Parkinson's disease (PD) by including a more detailed assessment of exposure to the chemicals for analyzing dose-effect relationships, especially for different classes of insecticides, fungicides, and herbicides, as well as examining the role of genetic traits in determining individual susceptibility to PD.

Dr. Alexis Elbaz of the Institut National de la Santé et de la Recherche Médicale, Paris, and his colleagues conducted extensive in-person interviews about professional exposure to pesticides with 247 patients with PD and 676 matching control patients. All of the participants came from the same French health insurance organization for workers in agriculture and related occupations. The patients with PD had been diagnosed a median of 1.5 years before the study (*Ann. Neurol.* 2009 [doi:10.1002/ana.21717]).

Dr. Elbaz and his associates found that for men, the odds of developing PD increased with the number of years of professional use of pesticides. This relationship was stronger for men with PD onset after age 65 years than it was for men with younger onset. Women with pesticide exposure also were significantly more likely to develop PD than were those without exposure.

Of the three broad categories of pesticides that the investigators analyzed—insecticides, fungicides, and herbicides—only insecticide exposure in men was associated with a significantly increased odds of developing PD (odds ratio 2.2). This association followed a dose-effect relationship, which was strongest for older-onset PD pa-



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tients. In women, only fungicide exposure was associated with significantly increased odds of developing PD (odds ratio 3.5). In multivariate analyses of men overall and of men with older-onset PD, only organochlorine insecticides remained associated with PD after adjusting for other pesticide families that the men had been exposed to.

During 1941-1990, patients with older-onset PD had used organochlorines in each 10-year period more often than their matched controls had, whereas there was no difference in use during the same periods between patients with younger-onset PD and their matched controls. Each control group used organochlorines, as well as insecticides and pesticides, at similar frequencies.

The finding that the association between PD and professional pesticide use was stronger for older males is "consistent with the view that genetic susceptibility plays a stronger role in younger-onset cases, while environmental factors play a stronger role for older-onset cases," the investigators wrote.

In a separate study, Dr. Ruey-Meei Wu of the department of neurology at National Taiwan University Hospital, Taipei, and her colleagues genotyped 125 patients (69 women) with sporadic idiopathic PD and 162 age- and gender-matched control patients (90 women) from a rural area of southern Taiwan for four glutathione S-transferase (GST) genes (GSTM1, GSTP1, GSTT1, and GSTZ1). Overall, 69 PD patients and 70 control patients were exposed to pesticides (herbicides, insecticides, and fungicides) used in professional farming or gardening. These patients had been exposed to pesticides for a range of 1 to 50 years. Dr. Wu and her colleagues reported at a poster session of the International Congress of Parkinson's Disease and Movement Disorders in Paris.

GST polymorphisms have been reported to reduce the efficiency of the substrate selectivity or stability of the enzymes. In brain tissue, GSTs function as scavengers that eliminate the formation of intracellular free radicals that are generated from the metabolism of drugs, toxins such as pesticides, or xenobiotics. GSTs have the potential to modify a person's susceptibility to developing PD after pesticide exposure by increasing oxidative stress in the brain, leading to the degeneration of dopaminergic neurons, Dr. Wu said in an interview.

Pesticide exposure was an independent risk factor for PD. Only the GSTP1 Val 105 polymorphism, which occurred in about 20% of the patients, significantly increased the risk for the development of PD. This polymorphism raised the odds of developing PD by a factor of 2.2. The risk for PD was greatest among patients who had been exposed to pesticides for more than 35 years.

Those who carried the GSTP1 Val 105 polymorphism and were exposed to pesticides had even higher risk of developing PD. There was a trend for increasing PD risk that became stronger and more significant in pesticide-exposed patients who carried an additional putative high-risk GST genotype.

None of the investigators in either study had any conflicts of interest to declare. ■

Pilot Study Shows Feasibility of Telemedicine for Parkinson's

BY RENÉE MATTHEWS

Using telemedicine to evaluate patients with Parkinson's disease is reliable and feasible, according to data from a small, randomized, controlled pilot study of nursing home and community-dwelling patients.

Patients in the study with Parkinson's disease (PD) who received telemedicine care over the course of 6 months showed improvements in quality of life, mood, satisfaction with care, cognition, and motor function, compared with those who received standard care, Dr. Kevin M. Biglan and Dr. Ray Dorsey of the University of Rochester (N.Y.) and their colleagues reported at the International Congress of Parkinson's Disease and Movement Disorders in Paris.

They also reported that tele-video assessments of the motor Unified Parkinson's Disease Rating Scale (UPDRS) were reliable and valid, compared with the standard in-person assessments of these patients.

The researchers enrolled 14

patients who lived 150 miles from the university (4 in a nursing home and 10 who lived in the community nearby). By providing the patients with Web-based telemedicine, they sought to improve their access to specialized care. They also hoped to be able to use telemedicine to expand the pool of Parkinson's patients who could participate in clinical trials if the logistics and difficulties relating to travel and costs were eliminated.

At baseline, the participants were a mean age of 71 years, and half were women. They had a mean Hoehn & Yahr stage of 2.7 (range, 1-5) and a mean motor UPDRS of 34.7 (range, 1-108, with higher scores indicating greater disability).

The community participants were randomized to telemedicine care (six) or standard care (four). All four nursing home patients received telemedicine care. Those in the telemedicine group received three one-on-one visits over 6 months (month 1, 2, and 3) from one of two investigators who were movement disorder

specialists. There was a fourth visit, at 6.5 months, to allow for the test-retest reliability comparison of the 6- and 6.5-month motor scores.

The Web-based televideo assessments were conducted at the nursing home. They mirrored an in-person evaluation, during which patients were asked about their PD, medications, function, and complications of therapy. The investigator performed a motor UPDRS examination at each visit, with a nurse available to assist in performing rigidity testing and pull testing.

Participants in the control group received their standard routine care from their primary physician and/or neurologist.

All the community-dwelling patients randomized to telemedicine completed all three telemedicine visits. Compared with their standard-care counterparts, they showed significant improvements in quality of life on the EQ-5D (6.3-point improvement vs. 17.2-point deterioration) and the motor UPDRS (0.33 improvement vs. 6.5 dete-

rioration). The four nursing home patients completed 94% of their telemedicine visits, showing trends toward improvement in care satisfaction, quality of life, and depressive symptoms.

The investigators also reported the motor UPDRS items were able to be completed at each visit. All of the motor items were fair or better agreement between telemedicine and in-person, except for rigidity and leg agility, leading the researchers to conclude that the motor UPDRS is reliable and valid in the telemedicine setting.

One of the 10 telemedicine participants discontinued with telemedicine care after the study was completed.

In focus group follow-up, both patients and caregivers reported high satisfaction with telemedicine, "especially the decreased travel burden and access to higher quality, dedicated PD experts," Dr. Biglan said in an interview. "They were adamant that it was convenient and made communicating easy." Nevertheless, "travel remained an issue for some,

[and] others had mixed feelings about completing telemedicine visits at home without medical and technical support staff."

Dr. Biglan said the study was limited by its focus on feasibility and a single disease. "While short-term feasibility was established, the long-term feasibility and benefits of telemedicine [have yet] to be evaluated. The study's focus was PD, whose clinical evaluation is largely visual. The reliability and validity of telemedicine assessments for PD remains to be established, as does applicability to other conditions such as Alzheimer's disease, which are more common in nursing home populations."

The researchers plan to expand the telemedicine initiatives to other sites and evaluate the use of remote assessments via telemedicine in clinical trials.

The study was funded by the Presbyterian Home for Central New York and the Central New York Parkinson's Disease Support Group. None of the researchers had any conflicts of interest. ■